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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/657,075	09/09/2003	Dennie J.M. van den Heuvel	SYN-0031D1	9183

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MARK R. BUSCHER
P.O. BOX 161
CATHARPIN, VA 20143

EXAMINER	
CHOI, FRANK I	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 08/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/657,075	VAN DEN HEUVEL ET AL.	
	Examiner	Art Unit	
	Frank I. Choi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *41-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 41-43, 51, 57-59 rejected under 35 U.S.C. 102(b) as being anticipated by Heafield et al. (US Pat. 4,867,985).

Heafield et al. expressly discloses a process for preparing a spheroid containing 500 gm active agent, 400 gms microcrystalline cellulose and 92.5 gm lactose and 7.5 grms hydroxyl propopyl cellulose which is mixed with 500 ml of water, extruded and spherioised, which spheroids are dried and have a 1 to 1.4 mm diameter or 220 gms active ingredient, 760 gm microcrystalline cellulose, 20 gm hydroxypropyl cellulose was mixed with 700 ml water to form a granulated mass which was extruded, which extrudate was spherioised and which speroids were dried and sieved to obtain 1.0 to 1.4 diameter size (column 3, lines 50-68, Column 4, lines 31-43).

Claims 41-43, 46, 51, 57, 59 are rejected under 35 U.S.C. 102(b) as being anticipated by JP 06-056700.

JP 06-056700 expressly discloses a process of preparing a spherical granule by combining water, pharmaceutical and crystalline cellulose in a stirring type granulator having a agitator and chopper and taking the granule prepared and obtaining the particle size distribution by using sieves (Paragraphs 0029-0030, 0034, 0035).

Claims 41-44, 49, 51, 57-59 rejected under 35 U.S.C. 102(b) as being anticipated by WO 98/10754.

WO 98/01754 discloses a process of preparing a rounded pellet having a mesh size of 0.6-1.25 mm by mixing carvedilol and microcrystalline cellulose and granulating in 3500 ml of distilled water, extruding and forming pellets in a rounder, drying on a fluidized bed and screening the pellets (Pgs. 11-19, 21). See US Pat 6, 224,909 for English language version.

Claims 41-49,57-59 are rejected under 35 U.S.C. 102(b) as being anticipated by Oren et al. (US Pat. 4,753,801).

Oren et al. expressly discloses mixing in a Diosna mixer a pharmaceutical agent, carrier for five minutes at low mixer and chopper sped settings while adding 6563 ml of a 15% aqueous povidone solution added slowly, then mixing at high speed mixer and chopper settings for three minutes while adding sufficient purifed water to produce a satisifactory granulation which was wet sieved through a no. 6 screen and dried at 110 degrees Fahrenheit and is spherical (Column 4, lines 14-26, Column 5, lines 35-51).

Claims 41-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP 06-056700 in view of Patel et al. (US Pat. 6,248,363) and Wear et al. (US Pat. 4,640,020).

JP 06-056700 discloses a process of preparing a spherical granule by combining water, pharmaceutical and crystalline cellulose in a stirring type granulator having a agitator and

chopper and taking the granule prepared and obtaining the particle size distribution by using sieves (Paragraphs 0008-0030, 0034, 0035). It is disclosed that extrusion did not result in uniform sphericity and that spraying involved a long process and for fine grains had bad coating effectiveness (paragraphs 0004,0005). It is disclosed that a 850 micrometer sieve can be used to separate the spherical granules (Paragraph 0014).

Patel et al. discloses methods of preparing pellets by combining solvent, such as water, pharmaceutically active agent, such as tamulosin, venlafaxine, zolpidem or zoplicone or salt thereof, and microcrystalline cellulose and drying through utilizing appropriate drying processes such as vacuum evaporation, heating etc. (Column 6, lines 1-11, Column 36, lines 40,Column 45, lines 40-68, Column 46, lines 16-62).

Wear et al. discloses a process and apparatus for drying granular or nodular products, such as pharmaceuticals using microwave energy which is especially suitable for drying temperature sensitive products (Column 1, lines 5-16, Column 2, lines 38-40). It is disclosed that nitrogen gas is used to purge the moisture driven from the product (Column 11, lines 34-53).

The difference between the prior art and the claimed invention is that the prior art does note expressly disclose the rate of dumping of water, the time period of stirring and/or chopping, the active agents claimed and the average diameter claimed. However, the prior art amply suggests the same as processes for forming pellets are disclosed by the cited prior art including the process described above. As such, it would have been well within the skill of one of ordinary skill in the art to modify the prior art as desired with the expectation that the process would form suitable pharmaceutical pellets and to use any pharmaceutical agent as desired depending on end use of the pellet.

Examiner has duly considered Applicant's arguments but deems them unpersuasive.

Although Patel does teach a process which uses spray nozzles, said process is not essential to the formation of spherical granules. JP '700 does not spray or use a flow restricting device. Applicant's specification describes flow restriction as not using a flow restricting device, however, said definition does not preclude varying degrees of flow. For example, the flow level in JP'700 is quantum dropping. Applicant's own Specification indicates that the solvent can be added in discrete dumps or all at once (Pg. 14 „ lines 18-21) Further, JP'700 is not limited to less than 400 micrometers and disclose the use of a 850 micrometer sieve to separate the spherical granules (Paragraph 0014). The formation of spherical granules is not surprising as JP '700 discloses a process of formulating the same falling within the scope of Applicant's claims.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Claims 41-53, 57-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oren et al. (US Pat. 4,753,801), Wear et al. (US Pat. 4,640,020), Giercksky et al. and Mosby's Gen Rx (8^{th} Ed. 1998).

Oren et al. discloses mixing in a Diosna mixer a pharmaceutical agent, carrier for five minutes at low mixer and chopper sped settings while adding 6563 ml of a 15% aqueous povidone solution added slowly, then mixing at high speed mixer and chopper settings for three minutes while adding sufficient purifed water to produce a satisifactory granulation which was wet sieved through a no. 6 screen and dried at 110 degrees Fahrenheit and is spherical (Column 4, lines 14-26, Column 5, lines 35-51). It is disclosed that the formulations contain about 15%

by weight of microcrystalline cellulose and up to about 80% of an active agent (Column 1, lines 23,24, Column 2, lines 33, 39).

Wear et al. discloses a process and apparatus for drying granular or nodular products, such as pharmaceuticals using microwave energy which is especially suitable for drying temperature sensitive products (Column 1, lines 5-16, Column 2, lines 38-40). It is disclosed that nitrogen gas is used to purge the moisture driven from the product (Column 11, lines 34-53).

Giercksky et al. discloses that zopiclone is a hypnotic (Abstract).

Mosby's Gen Rx (8th Ed. 1998) discloses that tamsulosin is used to treat benign prostatic hyperplasia, venlafaxine is used to treat depression and zolpidem is a hypnotic (Pgs. II-2019, 2020, 2183, 2219).

The difference between the prior art and the claimed invention is that the prior art does not expressly disclose drying under reduced pressure while passing nitrogen gas over the wet granules and applying microwave energy, the use of microcrystalline cellulose, or the claimed pharmaceutically active agents. However, the prior art amply suggests the same as processes for forming pellets are disclosed by the cited prior art including the process described above. As such, it would have been well within the skill of one of ordinary skill in the art to modify the prior art as desired with the expectation that the process would form suitable pharmaceutical pellets and to use any pharmaceutical agent as desired depending on end use of the pellet.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Claims 41-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heafield et al. (US Pat. 4,867,985) in view of Wear et al. (US Pat. 4,640,020), Giercksky et al. and Mosby's Gen Rx (8th Ed. 1998).

Heafield et al. expressly discloses a process for preparing a spheroid containing 500 gm active agent, 400 gms microcrystalline cellulose and 92.5 gm lactose and 7.5 grms hydroxyl propopyl cellulose which is mixed with 500 ml of water, extruded and sphernoised, which spheroids are dried and have a 1 to 1.4 mm diameter or 220 gms active ingredient, 760 gm microcrystalline cellulose, 20 gm hydroxypropyl cellulose was mixed with 700 ml water to form a granulated mass which was extruded, which extrudate was sphernoised and which speroids were dried and sieved to obtain 1.0 to 1.4 diameter size (column 3, lines 50-68, Column 4, lines 31-43).

Wear et al. (US Pat. 4,640,020), Giercksky et al. and Mosby's Gen Rx (8th Ed. 1998) are cited for the same reasons as above and are incorporated herein to avoid repetition.

The difference between the prior art and the claimed invention is that the prior art does not expressly disclose the rate of adding water, adding water during the mixing/chopping process, the time of the granulation process, drying under reduced pressure while passing nitrogen gas over the wet granules and applying microwave energy or the claimed pharmaceutically active agents. However, the prior art amply suggests the same as processes for forming pellets are disclosed by the cited prior art including the process described above. As such, it would have been well within the skill of one of ordinary skill in the art to modify the prior art as desired with the expectation that the process would form suitable pharmaceutical pellets and to use any pharmaceutical agent as desired depending on end use of the pellet.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Conclusion

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier number for accessing the facsimile machine is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Choi whose telephone number is (571)272-0610. Examiner maintains a flexible schedule. However, Examiner may generally be reached Monday-Friday, 8:00 am – 5:30 pm (EST), except the first Friday of the each biweek which is Examiner's normally scheduled day off.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Mr. Gary Kunz, can be reached at 571-272-0887. Additionally, Technology Center 1600's Receptionist and Customer Service can be reached at (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

FIC
August 22, 2005

SABIHA QAZI, PH.D
PRIMARY EXAMINER